

Claims

1. A method for preparing a target substance in particulate form, the method comprising introducing into a particle formation vessel, through separate first and second fluid inlets respectively, (a) a solution or suspension of the target substance in a fluid vehicle (the “target solution/suspension”) and (b) a compressed fluid anti-solvent for the substance, and allowing the anti-solvent fluid to extract the vehicle from the target solution/suspension so as to form particles of the target substance, wherein the target solution/suspension enters the vessel downstream of the point of entry of the anti-solvent fluid and at a point which lies on or close to the main axis of anti-solvent flow out of the second fluid inlet, and wherein the anti-solvent fluid has a sub-sonic velocity as it enters the particle formation vessel.
2. A method according to claim 1, wherein the target solution/suspension and the anti-solvent meet immediately downstream of the point of anti-solvent entry into the particle formation vessel.
3. A method according to claim 1 wherein the target solution/suspension and the anti-solvent meet within 0.001 to 0.1 milliseconds of the anti-solvent entering the particle formation vessel.
4. A method according to claim 1, wherein the Mach number of the anti-solvent fluid as it enters the particle formation vessel (ie, the ratio of its actual speed to the speed of sound in that fluid at that point) is 0.7 or lower.
5. A method according to claim 4, wherein the Mach number of the anti-solvent fluid as it enters the vessel is from 0.05 to 0.5.
6. A method according to claim 1, wherein the anti-solvent is a supercritical or near-critical fluid.
7. A method according to claim 1, wherein the anti-solvent fluid is carbon dioxide.

8. A method according to claim 1, wherein the target substance comprises a pharmaceutical or pharmaceutical excipient.
9. A method according to claim 1, wherein the second fluid inlet comprises a nozzle.
- 5 10. A method according to claim 9, wherein the nozzle is a convergent nozzle which focuses the anti-solvent flow through a smaller area outlet.
11. A method according to claim 1, wherein the outlet of the second fluid inlet has a diameter from 0.1 to 0.5 mm.
12. A method according to claim 1, wherein the target solution/suspension is
10 introduced into the particle formation vessel with a back pressure.
13. A method according to claim 1, wherein the target solution/suspension is introduced directly into the anti-solvent flow, and meets with the anti-solvent flow at the point where the target solution/suspension enters the vessel.
14. A method according to claim 1, wherein the separation between (a) the outlet of
15 the first fluid inlet and (b) the main axis of anti-solvent flow (measured in a plane perpendicular to that axis) is no more than 10 times the diameter of the outlet of the second fluid inlet.
15. A method according to claim 1, wherein the centers of the outlets of the first and
20 second fluid inlets are both positioned on the central longitudinal axis of the second fluid inlet and/or along the main axis of anti-solvent flow.
16. A method according to claim 1, wherein the outlet of the first fluid inlet is located vertically below that of the second fluid inlet, and the anti-solvent fluid flows into the particle formation vessel in a vertically downwards direction.

17. A method according to claim 1, wherein the separation between the outlets of the first and second fluid inlets is from 15 to 25 times the diameter of the outlet of the second fluid inlet.
18. A method according to claim 1, wherein at the point where the target solution/suspension and the anti-solvent meet, the angle between their axes of flow is from 70 to 110 °.
19. A method according to claim 1, wherein the first fluid inlet has an outlet of diameter less than 0.2 mm.
20. A method according to claim 19, wherein the first fluid inlet has an outlet of diameter less than 0.1 mm.
21. A method according to claim 20, wherein the first fluid inlet comprises an outlet tube section having an outlet diameter of less than 0.1 mm, mounted in fluid communication with a wider diameter tube section through which the target solution/suspension may be directed from its source towards the outlet tube section and then to the particle formation vessel.
22. A method according to claim 1, wherein the outlet of the first fluid inlet has a smaller cross sectional area than that of the second fluid inlet.
23. A method according to claim 22, wherein the outlet of the first fluid inlet has a cross sectional area which is less than 50 % as large as that of the second fluid inlet.
24. A method according to claim 23, wherein the outlet of the first fluid inlet has a cross sectional area which is less than 2 % as large as that of the second fluid inlet.
25. A method according to claim 1, wherein the volumetric ratio of the target solution/suspension flow rate to the anti-solvent flow rate (both measured at or

immediately prior to the two fluids coming into contact with one another) is from 0.005 to 0.2.

26. A method according to claim 1, which additionally involves collecting the particles following their formation, within the particle formation vessel.